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Electrically Heated Cigarette Smoking System

Overview of JLI EHCSS

SAB Meeting
Washington, November 7-8, 2001

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Product Attributes

- Reduced smoke constituents identified as potentially harmful by public health authorities
- No sidestream smoke
- No ash
- Reduced odor
- No burning between puffs
- Reduced risk of fires from carelessly handled lit-end cigarettes

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Major Learning's Since Launch

- In both countries (USA & JP), reasons for discontinuing or situational use are:
  - Primarily Taste-related
    - High resistance to draw
    - Perceived harshness
    - Not enough taste
    - Not enough puffs per cigarette
  - Inconvenience
    - Charging time
    - Cigarette per charge
    - Break-off of the cigarette

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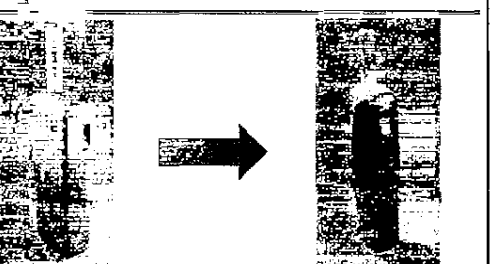
Lighter Evolution



Current Market (E4)
08/1998 Richmond
01/1999 Osaka

JLI
Formaldehyde Reduction
Improved Draw
Improved Shape

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Series E4 Heater

- E4
  - Electrical Cleaning
  - Rear Entry Air
  - RTD of System Controlled by Heater
  - First Puff Relief
  - 14mm Burn Length
  - 8 mil Blade Thickness
  - Product ID

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Series JLI Heater

- JLI
  - Water Cleanable
  - Sealed Cigarette End
  - Directed Front Entry Air (Air Channel Insert)
  - 14mm Burn Length
  - 8 mil Blade Thickness
  - Product ID

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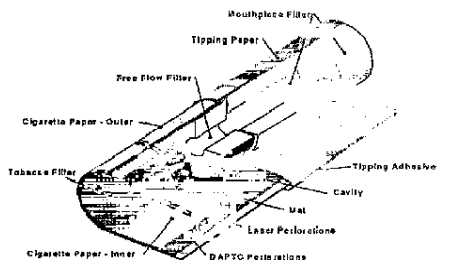
JLI Cigarette

Cigarette Construction



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Lighter Attributes Comparison

Commercial Product

Change Area	Current Market (E4)	JLI
Total Energy	23.1 Joules	23.7 Joules
Heater Energy Control	8 msec pulse width	4 msec pulse width
Preheat	Fixed on time (no energy control)	Fixed Joules (energy control-ed) 5 Joules / Blade
System RTD	RTD controlled by Heater 97 mm RTD	RTD controlled by sealing the cigarette in the lighter (cup in post) 25 mm RTD
Air Flow Control	Fill in Heater	Air Holes in Heater Internal Air Channel Insert (Metal) with slots to accommodate shoehorns
Latency	300 msec	130 msec
Puff Sensor Trigger	25mm H_2O	5mm H_2O
Puff Sensor Delay Software	70 msec.	40 msec.
Heater Cleaning System	Electric heater with catalyst	Hand Operated Brush Unit
Battery Capacity	Full power for 13 cigarettes (8 puffs)	Full Power for 19 cigarettes (8 puffs each) Reduced idle current Reduced circuit losses Sleep Mode

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Cigarette Attributes Comparison

Commercial Product

Change Area	Current Market (E4)	JLI
Mat Composition	170 gsm Basis Weight 9.0% Glycerin	205 gsm Basis Weight 10.5% Glycerin
Cigarette Configuration	82 mm Overall Length 32 mm Tobacco Rod 30 mm Filter Rod Mat Perforation Only	85 mm Overall Length 32 mm Tobacco Rod 36 mm Filter Rod Mat Perforation Cigarette Perforation
Cigarette Paper	CaCO3 Filler (30%) with Citrate 28 gsm Basis Weight 49 C Porosity	AMP Monohydrate (30%) 25 gsm Basis Weight 25 C Porosity
Cut Filler	283 mg/ cig	208 mg/cig
RAT ID	3.95 mm	3.3 mm

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Test Lighter Comparison

Change Area	"EHCSS-F"	"EHCSS-JLI"
Lighter Body	Modified E4 Lighter	Bridging Study Lighter
WSA Study	Hydra Inhalation Study	Hydra Bridging Study
Total Energy	23.8 Joules	23.7 Joules
Heater Energy Control	8 msec pulse width	4 msec pulse width
Preheat	2 cycles @0.125 sec / Blade full power	Fixed Joules (energy controlled) 5 Joules / Blade
System RTD	RTD controlled by sealing the cigarette in the lighter (cup in post) 25 mm RTD	RTD controlled by sealing the cigarette in the lighter (cup in post) 25 mm RTD
Air Flow Control	Air Holes in Heater Internal Air Channel Insert (PEEK)	Air Holes in Heater Internal Air Channel Insert (Metal) with Slots to accommodate shoehorns
Latency	300 msec	80 msec
Puff Sensor Trigger	25mm H_2O	1 mm H_2O
Puff Sensor Delay Software	70 msec	40 msec.

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Test Cigarette Comparison

Change Area	EHCSS-CaCO3-F	EHCSS-AMP-F	EHCSS-AMP-JLI
Mat Composition	205 gsm Basis Weight 10.5% Glycerin	No Change	No Change
Cigarette Configuration	83 mm Overall Length 32 mm Tobacco Rod 36 mm Filter Rod Mat Perforation Cigarette Perforation	No Change	No Change
Cigarette Paper	CaCO3 Filler (30%) 28 gsm Basis Weight 49 C Porosity	AMP Monohydrate (30%) 28 gsm Basis Weight 25 C Porosity	No Change
Cut Filler	208 mg/cig	No Change	No Change

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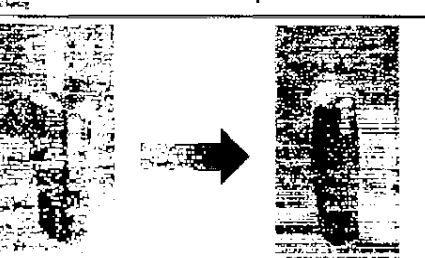
EHCSS Product Improvements



Current Market (E4)
08/1998 Richmond
01/1999 Osaka

JLI
80% Formaldehyde Reduction (ug/cig)
Improved Draw
Improved Shape

Proposed Agenda

- Overview of Philip Morris' Reduced Harm Program
- Clinimetrics Overview
- Clinimetrics General Monitoring Plan
- Clinimetrics Findings
- Query Resolution
- General Discussion

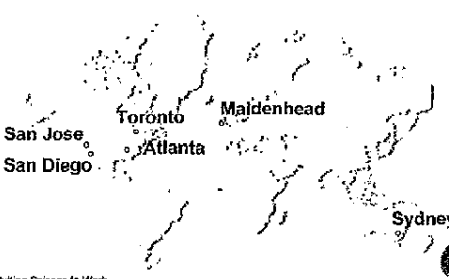
Putting Science to Work

Clinimetrics

A Global, Full-Service CRO

Putting Science to Work

Global Presence



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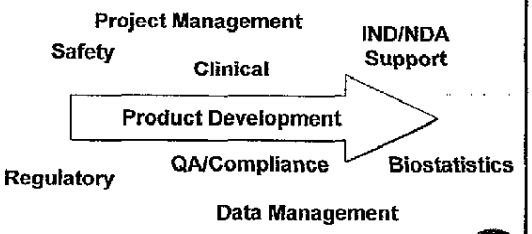
Full Service Capabilities



Putting Science to Work

Qualified Staff

- 330 Worldwide Employees
  - 59 Project Management
  - 140 Clinical
  - 52 Biometrics
  - 9 Medical Safety/Quality Assurance
  - 70 Professional and Support
- Experience
  - Average 6 Year Clinical Research Experience
  - Over 80% Hold Graduate Degrees and / or Clinical Certifications (R.N., P.A., R.Ph., M.D., etc.)
  - Multi-lingual

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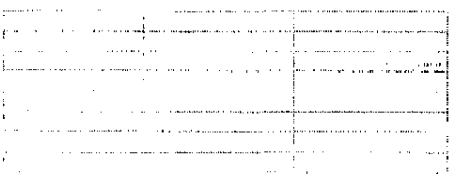
Confidence In Working With Clinimetrics

- Private, profitable since inception
- Lean, informal management structure
- Efficient decision-making
- Collaborative culture, encourage open/proactive communication
- Employee owned, low staff turnover (<12%)
- 80% of revenue from repeat business
- "Quality partnerships"

Putting Science to Work

Therapeutic Experience



Putting Science to Work

Philip Morris Experience

- 7 US studies:
  - 466-03
  - 466-04
  - 466-05
  - 473-01
  - 473-02
  - 473-03
  - 473-04

Putting Science to Work

Commitment

- Experienced Professional Staff
- Dedication to Client's Objectives and Timelines
- Accountable Project Management System
- Emphasis on Communications, Planning and Problem Solving

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Monitoring Approach for Philip Morris

- Good Clinical Practice/ICH Guidelines
- Monitoring Responsibility
- Monitoring
  - General
  - Protocol specific

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Good Clinical Practice (GCP)

- What is GCP?
  - ICH Guidelines
  - US Code of Federal Regulations (CFR)
- Who is responsible?
  - Sponsor
  - Investigator
  - Monitor

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Good Clinical Practice

GCP is a standard for the design, conduct, performance, monitoring, auditing, recording, analysis, and reporting of clinical trials.

- What is the purpose?
  - To protect the rights, safety, and well-being of the patient or study participant
  - To insure the data collected and conclusions drawn are accurate and credible

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History of Regulations

- ICH Guidelines, May 1997
  - Adopted by the EU, Japan, and the US
  - Improve quality and reliability of data
  - Study could be conducted using the same standards
  - Studies conducted under a US IND must also comply with FDA regulations, CRF-Title 21, Parts 11, 50, 54, 56, 312, and 314

Putting Science to Work

Responsibility of Clinimetrics

- Monitor progress of study in accordance with
  - Protocol
  - FDA Code of Federal Regulations
  - ICH GCP guidelines
  - SOPs

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Responsibility of Clinimetrics (cont.)

- IRB Approval and Correspondence
- Informed Consent Form
- Source Document Verification
- Investigational Product

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Monitoring of Philip Morris protocols

- Assist site in establishment of SOPs to enhance study conduct
- Proactive resolution of discrepancies
- Site GCP training

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Clinimetrics Monitoring Plan

- Purpose
- Monitoring Overview
- CRA Administrative Responsibilities
- Data Review
- Regulatory Documents Review
- Drug Accountability Review
- SAE Reporting

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Common Discrepancies

- Transcription errors
- Protocol deviations
  - Inclusion/Exclusion
  - Use of forbidden medication, non-study cigarettes, non-study lighter
- Obtaining informed consent

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Clinimetrics and MDS Pharma

- Synergy developed
  - Mutual respect for professional abilities and judgments
  - Willingness to exchange ideas and learn from one another
  - Shared commitment to do excellent research

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Project No. EHCJLI/01/02 (466-03)

- Closed: July 2002
- First study presented the biggest challenges
  - Study completed prior to Clinimetrics involvement
  - Regulatory Binder
  - Informed consent process
  - Topography devices
  - Product accountability

Putting Science to Work

Project No. EHCJLI/02/02 (466-04)

- Ongoing: monitoring to complete 3Q 2003
- Improvements
  - Product accountability
  - Informed consent process
- Challenges
  - Higher drop rate
  - Questionnaires
  - Accessibility to printed data

Putting Science to Work

Project No. EHCJLI/03/02 (466-05)

- Close-out scheduled: March 31-April 1, 2003
- Challenges
  - Study conducted at PAREXEL-Baltimore CPRU
  - 3rd cohort was added resulting in timeline shifts
  - Change in management staff
  - Topography device malfunctions
  - Accessibility to data

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Project No. SCoR2003-6/01/02 (473-01)

- Close-out visit completed: February 2003
- Very clean study
  - Minor ICF issues
  - Collection of topography data improved

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Project No. SCoR2003-6/02/02 (473-02)

- Subject completion on February 10, 2003
- Initial review of CRFs delayed until March 10, 2003
- To date
  - Complete ICF review
  - Complete product accountability
  - Screening questionnaire
- Complete monitoring in early April 2003

Putting Science to Work

Project No. SCoR2003-11/01/03 (473-03)

- Awarded in December 2002
- Subjects started/completed in January 2003
- To date:
  - Complete ICF review
  - Complete product accountability

Putting Science to Work

Project No. SCoR2003-11/02/03 (473-04)

- Awarded in December 2002
- Enrollment in January 2003
- To date:
  - Complete ICF review
  - Initial regulatory review

Putting Science to Work

Working Globally

Working Locally

Working Science